

| | | | | | |
|---|---|----|--------------------------|------------------------|---------|
| Substitute for form 1449/PTO | | | Complete if Known | | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT (Use as many sheets as necessary) | | | Application Number | 10/551,643-Conf. #5446 | |
| | | | Filing Date | July 24, 2006 | |
| | | | First Named Inventor | Giovanni Monteleone | |
| | | | Art Unit | 1645 | |
| | | | Examiner Name | Not Yet Assigned | |
| Sheet | 1 | of | 3 | Attorney Docket Number | GIU-001 |

| U.S. PATENT DOCUMENTS | | | | | |
|-----------------------|----------|---|--------------------------------|--|---|
| Examiner Initials* | Cite No. | Document Number Number-Kind Code ² (if known) | Publication Date MM-DD-YYYY | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear |
| | A1* | US-5,654,004 | 08-05-1997 | Okayama et al. | |
| | A2* | US-5,783,566 | 07-21-1998 | Mislick | |
| | A3* | US-5,929,226 | 07-27-1999 | Padmapriya et al. | |
| | A4* | US-6,096,722 | 08-01-2000 | Bennett et al. | |
| | A5* | US-6,159,697 | 12-12-2000 | Monia et al. | |
| | A6* | US-6,200,602 | 03-13-2001 | Watts et al. | |
| | A7* | US-6,251,628 | 06-26-2001 | Nakao et al. | |
| | A8* | US-6,455,689 | 09-24-2002 | Schlingensiepen et al. | |
| | A9* | US-6,479,465 | 11-12-2002 | Strober et al. | |
| | A10* | US-6,605,443 | 08-12-2003 | Nakao et al. | |
| | A11* | US-6,794,367 | 09-21-2004 | Tanida et al. | |
| | A12* | US-6,884,787 | 04-26-2005 | Monia et al. | |
| | A13* | US-6,943,241 | 09-13-2005 | Isogai et al. | |
| | A14* | US-20020177568 | 11-28-2002 | Stinchcomb et al. | |
| | A15* | US-20050119203 | 06-02-2005 | Steinbrecher et al. | |
| | A16* | US-20070042985 | 02-22-2007 | Monteleone | |

| FOREIGN PATENT DOCUMENTS | | | | | | |
|--------------------------|----------|---|------------------|---|---|----------------|
| Examiner Initials* | Cite No. | Foreign Patent Document | Publication Date | Name of Patentee or Applicant of Cited Document | Pages, Columns, Lines, Where Relevant Passages Or Relevant Figures Appear | T ³ |
| | | Country Code ¹ -Number ¹ -Kind Code ² (if known) | MM-DD-YYYY | | | |
| | B1 | WO-08/014400 | 01-31-2008 | Genizon Biosciences Inc et al. | | ✓ |
| | B2 | WO-99/050296 | 10-07-1999 | Eli Lilly and Company | | ✓ |

| | |
|--------------------|-----------------|
| Examiner Signature | Date Considered |
|--------------------|-----------------|

*EXAMINER Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant. * CITE NO. Those application(s) which are marked with a single asterisk (*) next to the Cite No. are not supplied (under 37 CFR 1.99(a)(2)(iii)) because that application was filed after June 30, 2003 or is available in the IFW. ¹ Applicant's unique citation designation number (optional). ² See Kinds Codes of USPTO Patent Documents at www.uspto.gov or MPEP 901.04. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST.16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

| NON PATENT LITERATURE DOCUMENTS | | | | | |
|---------------------------------|-----------------------|---|--|--|----------------|
| Examiner Initials* | Cite No. ¹ | Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published. | | | T ³ |
| | C1 | Agrawal, S., et al., "Antisense Therapeutics: Is it as Simple as Complementary Base Recognition?", Molecular Medicine Today, February 2000 (Vol. 5), pps. 72-81. | | | |
| | C2 | Arsuru, M., et al., "TGFβ1 Inhibits NF-κB/Rel Activity Inducing Apoptosis of B Cells: Transcriptional Activation of IkBγ, Immunity, Vol. 5, 31-40, July, 1996. | | | |
| | C3 | Boirivant, M., et al., "Lamina Propria T Cells in Crohn's Disease and other Gastrointestinal Inflammation Show Defective CD2 Pathway-Induced Apoptosis," Gastroenterology, 1999: 116: 557-565. | | | |
| | C4 | Boirivant, M., et al., "Oral Administration of Recombinant Cholera Toxin Subunit B Inhibits IL- | | | |

| | | | |
|--|---|-------------------------------|------------------------|
| Substitute for form 1449/PTO | | Complete if Known | |
| INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i> | | Application Number | 10/551,643-Conf. #5446 |
| | | Filing Date | July 24, 2006 |
| | | First Named Inventor | Giovanni Monteleone |
| | | Art Unit | 1645 |
| | | Examiner Name | Not Yet Assigned |
| | | Attorney Docket Number | GIU-001 |
| Sheet | 2 | of | 3 |

| | | | |
|-----|---|--|---|
| | | 12-Mediated Murine Experimental (Trinitrobenzene Sulfonic Acid) Colitis," The Journal of Immunology, 2001. | |
| C5 | Boirivant, M., et al., "Oxazolone Colitis: A Murine Model of T Helper Cell Type 2 Colitis Treatable with Antibodies to Interleukin 4," The Journal of Experimental Medicine, Vol. 188, No. 10, November 16, 1998, 1929-1939. | | |
| C6 | Christ, M., et al., "Immune Dysregulation in TGF- β 1-Deficient Mice," The Journal of Immunology, 1994. | | |
| C7 | Fiocchi, C., "TGF- β /Smad Signaling Defects in Inflammatory Bowel Disease: Mechanisms and Possible Novel Therapies for Chronic Inflammation," The Journal of Clinical Investigation, Vol. 108, No. 4, August 2001. | | |
| C8 | Gorelik, L., et al., "Abrogation of TGF β Signaling in T Cells Leads to Spontaneous T Cell Differentiation and Autoimmune Disease," Immunity, Vol. 12, 171-181, February, 2000. | | |
| C9 | Gorelik, L., et al., "Transforming Growth Factor- β in T-Cell Biology," Nature Reviews/Immunology, Vol. 2, January 2002. | | |
| C10 | Guerlavais, T., et al., "Use of Maldi-TOF Mass Spectrometry to Monitor Solid-Phase Synthesis of Oligonucleotides," Anal Bioanal Chem (2002) 374: 57-63. | | |
| C11 | Hahn, K. B., et al., "Loss of Transforming Growth Factor β Signalling in the Intestine Contributes to Tissue Injury in Inflammatory Bowel Disease," Gut 2001;49: 190-198. | | |
| C12 | Han, Seung H., et al., "Transforming Growth Factor-Beta 1 (TGF- β 1) Promotes IL-2 mRNA Expression Through the Up-regulation of NF- κ B, AP-1 and NF-AT in EL4 Cells," The Journal of Pharmacology and Experimental Therapeutics, Vol. 287, No. 3. | | |
| C13 | Hayashi, H., et al., "The MAD-related Protein Smad7 Associates with the TGF β Receptor and Functions as an Antagonist of TGF β Signaling," Cell, Vol. 89, 1165-1173, June 27, 1997. | | |
| C14 | Heldin, Carl Henrik, et al., "TGF- β Signalling from Cell Membrane to Nucleus Through SMAD Proteins," Nature, Vol. 390, 4 December 1997. | | |
| C15 | Lawrance, Ian Craig, et al., "Inflammation Location, But Not Type, Determines the Increase in TGF- β 1 and IGF-1 Expression and Collagen Deposition in IBD Intestine," Inflammatory Bowel Diseases, Vol. 7, No. 1, February 2001. | | |
| C16 | Lawrance, Ian C., et al., "A Murine Model of Chronic Inflammation-Induced Intestinal Fibrosis Down-Regulated by Antisense NF- κ B," Gastroenterology 2003;125:1750-1761. | | |
| C17 | Lesiak, Krystyna, et al., "2',5'-Oligoadenylate: Antisense Chimeras--Synthesis and Properties," Bioconjugate Chem. 1993, 4, 467-472. | | |
| C18 | Ludviksson, B.R., et al., "TGF- β Production Regulates the Development of the 2,4,6-Trinitrophenol-Conjugated Keyhole Limpet Hemocyanin-Induced Colonic Inflammation in IL-2-Deficient Mice," The Journal of Immunology, 1997. | | |
| C19 | Maggi, A., Biotecnologie Farmacologiche, 1998, Cap. 8: 125-131. | | ✓ |
| C20 | Maier, Martin A., et al., "Synthesis of Chimeric Oligonucleotides Containing Phosphodiester, Phosphorothioate, and Phosphoramidate Linkages," Organic Letters 2000, Vol. 2, No. 13, p. 1819-1822. | | |
| C21 | Monteleone, G., et al., "Blocking Smad7 Restores TGF- β 1 Signaling in Chronic Inflammatory Bowel Disease," The Journal of Clinical Investigation, August 2001, vol. 108, No. 4, p. 601-609. | | |
| C22 | Neurath, M.F., et al., "Experimental Granulomatous Colitis in Mice is Abrogated by Induction of TGF- β -Mediated Oral Tolerance," J. Exp. Med., Vol. 183, June 1996, p. 2605-2616. | | |
| C23 | Neurath, M., et al., "TNBS-Colitis," Intern. Rev. Immunol., Vol. 19, p. 51-62. | | |
| C24 | Podolsky, D.K., "Inflammatory Bowel Disease," N. Engl. J. Med., Vol. 347, No. 6, August 8, 2002, p. 417-429. | | |
| C25 | Powrie, F., et al., "A Critical Role for Transforming Growth Factor- β but not Interleukin 4 in the | | |

| | | | | | |
|--|---|--------------------------|------------------------|------------------------|---------|
| Substitute for form 1449/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(Use as many sheets as necessary)</i> | | Complete if Known | | | |
| | | Application Number | 10/551,643-Conf. #5446 | | |
| | | Filing Date | July 24, 2006 | | |
| | | First Named Inventor | Giovanni Monteleone | | |
| | | Art Unit | 1645 | | |
| | | Examiner Name | Not Yet Assigned | | |
| Sheet | 3 | of | 3 | Attorney Docket Number | GIU-001 |

| | | | |
|--|-----|--|--|
| | | Suppression of T Helper Type 1-Mediated Colitis by CD45RBlow CD4+ T Cells," J. Exp. Med., Vol. 183, June 1996, p. 2669-2674. | |
| | C26 | Ragas, J.A., "A Comparative Study on Methods of Optimal Sample Preparation for the Analysis of Oligonucleotides by Matrix-Assisted Laser Desorption/Ionization Mass Spectrometry," Analyst, 2000, 125, p. 575-581. | |
| | C27 | Read, S., et al., "Induction of Inflammatory Bowel Disease in Immunodeficient Mice by Depletion of Regulatory T Cells," Current Protocols in Immunology (1999) 15.13.1-15.13.10. | |
| | C28 | Sanborn, et al., "Biologic Therapy of Inflammatory Bowel Disease," Gastroenterology 2002;122:1592-1608. | |
| | C29 | Sanghvi, Y.S., et al., "Antisense Oligodeoxynucleotides: Synthesis, Biophysical and Biological Evaluation of Oligodeoxynucleotides Containing Modified Pyrimidines," Nucleic Acids Research, 1993, Vol. 21, No. 14, 3197-3203. | |
| | C30 | Seegers, D., et al., "Review Article: A Critical Approach to New Forms of Treatment of Crohn's Disease and Ulcerative Colitis," Aliment Pharmacol Ther 2002; 16(Suppl. 4): 53-58. | |
| | C31 | Shull, M.M., et al., "Targeted Disruption of the Mouse Transforming Growth Factor- β 1 Gene Results in Multifocal Inflammatory Disease," Nature, Vol. 359, 22 October 1992, p. 693-698. | |
| | C32 | Wei, X., et al., "Synthesis and Characterization of Composite Nucleic Acids Containing 2',5'-Oligoriboadenylate Linked to Antisense DNA," Antisense & Nucleic Acid Drug Development 6:247-258 (1996). | |
| | C33 | Yang, X., "Targeted Disruption of SMAD3 Results in Impaired Mucosal Immunity and Diminished T Cell Responsiveness to TGF- β ," The EMBO Journal, Vol. 18, No. 5, pp. 1280-1291, 1999. | |

| | | | |
|--------------------|--|-----------------|--|
| Examiner Signature | | Date Considered | |
|--------------------|--|-----------------|--|

*EXAMINER Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Applicant's unique citation designation number (optional). ²Applicant is to place a check mark here if English language Translation is attached.